

Anti IH: An antibody worth mention

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Abstract:

A 72-year-old female with co-morbidities posted for surgical correction of fracture neck of femur without any history of transfusions was noted to have a hemoglobin level of 7 g/dl and packed red blood cells transfusion was ordered. Pretransfusion tests demonstrated A₁B group with D positive on forward grouping. Reverse grouping showed a varying grade of agglutination with A, B, and O cells. Agglutination being stronger at 4°C. Antibody screening showed pan-agglutination, direct Coomb's test and auto control were negative. The serum reacted with adult O cells (O_{I_{adult}}) but not with adult Bombay cells (Oh I_{adult}) or O cord (O_{I_{cord}}) cells. A possibility of a compound cold antibody anti IH was made and A₁B compatible cells were transfused to the patient. This case report illustrates anti-IH cold agglutinin with broad thermal amplitude. Uniqueness of this case report was O group incompatibility with A₁B group, which was detected earlier and a catastrophic transfusion reaction being subverted.

Key words:

Anti IH, Bombay Cells, compound antibody, O cord cells

Introduction

Anti-IH is a complex antibody which is commonly benign in nature with preferential action in cold temperature. The co-expression of both I and H antigens is required on the red blood cell for its manifestation. Anti-IH is seen in individuals with A₁B, A₁, and B blood groups. Its reactivity depends on the amount of H antigens on red cells, which makes it react more with O and A₂ cells when compared to A₁ and A₁B cells.^[1] Rarely anti-IH presents as a clinically significant antibody resulting in cold agglutinin syndrome and hemolytic transfusion reactions.^[2-7] This case describes a clinically significant anti-IH antibody with a wide thermal amplitude which was recognized during pretransfusion testing.

Case Report

A 72-year-old female with Type 2 diabetes, past history of cerebrovascular accident and pulmonary embolism on warfarin was admitted for surgical correction of fracture neck of femur. She was multiparous, with three surviving children and no previous history of any blood transfusion. Her investigation revealed hemoglobin of 7 g/dl which necessitated packed red blood cell (PRBC) transfusion.

Blood grouping by conventional tube testing (CTT) showed a discrepancy, forward grouping (Resolve antisera, Orthodiagnosics) suggesting AB, Rh (D) positive while reverse grouping showed varying grades of agglutination with A₁, B, and O cells [Table 1], where O cells showed a higher grade

of agglutination than B and A₁ cells, respectively. Reverse grouping repeated after incubating for 15 min at 4°C and 37°C [Table 2a and b] showed the antibody as having preferential action at lower temperatures, hence raising a suspicion of cold antibody. Reverse grouping at 37°C with a prewarmed sample showed a weak reaction. The subgroup of A antigen was confirmed as A₁ using anti-A₁ lectin (Tulip diagnostics). Antibody screening with the commercially available panel (Orthoclinical diagnostics 3-cell panel) revealed pan-agglutination at room temperature (RT) by CTT and grade of reaction weakened at 37°C (CTT) and with Coomb's phase [Table 3]. Direct Coomb's test and autocontrol were negative.

Cold antibody anti-I was ruled out as patients sera failed to show agglutination with Bombay cells (Oh I_{adult}, I antigen present but H antigen absent), while anti-H was ruled out as patient sera failed to show a reaction with cord cells (O_{I_{cord}}, H antigen present but I antigen absent). A 3+ reaction was obtained

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with serum during an immediate spin with A₂ cells while it was weak with A₁ cells [Table 4a]. The reaction patterns matched with cold autoantibody anti-IH. Titration studies at 4°C and 20–22°C showed titers 32 and 16, respectively. This broad thermal amplitude of anti-IH antibody makes it clinically significant. The patient's blood was found to be compatible with A₁B cells but not with O cells, as A₁B cells are known to have the least expression of H antigens, hence was transfused with compatible A₁B PRBCs and posttransfusion follow-up showed no derangement in patient's liver function tests or lactate dehydrogenase.

Discussion

Cold auto agglutinins are commonly found in human sera, mostly IgM antibodies with a very narrow thermal range and a low titer (<64) of activity making them clinically insignificant or benign.^[8,9] They are mostly directed against carbohydrate antigens, most commonly the Ii antigen.^[10] Antigenic similarity between various carbohydrate antigens contribute to the development of complex antibodies.^[8-11] Clinical significance of cold antibodies is mostly restricted to cold agglutinin syndrome and very rarely hemolytic reactions. They routinely express high titers (>1000) at 4°C and a high thermal amplitude.

The various cold autoantibodies described in, literature, are anti-I, anti-i, anti-H, compound antibody anti-IH.^[1]

This case provides a rare example of a clinically significant complex antibody with specificity against co-expression of I and H moiety. Anti-IH found more commonly in A₁, A₁B, and B blood group individuals, present as a benign antibody and have occasionally caused acute or delayed hemolytic reactions.^[2-7] The severity of hemolysis depends on the amount of H antigen substance hence follows the following order of reactivity O > A₂ > B > A₂B > A₁ > A₁B.^[12]

Unlike anti-H and anti-I antibodies, anti-IH reacts only in the presence of both antigens together. Agglutination with OI_{adult} cells and not with Oi_{cord} cells and Oh I_{adult} Bombay cells confirmed the specificity of anti-IH [Table 4b].^[1]

Thermal amplitude studies with a fresh prewarmed blood sample demonstrated reactivity at 37°C. Tests at 4°C and RT showed titer of 32 and 16, respectively with adult O cells. The wide thermal amplitude rather than titer is critical regarding the clinical significance of an antibody.^[8] Thermal amplitude and titration tests were done using only adult O cells. The reduction of the strength of reaction with prewarming is contributory to the absence of a clinically significant alloantibody. However, this statement is being guarded due to the observation that the reactivity of clinically significant alloantibodies can be weakened by prewarming.^[13,14]

Anti-IH can rarely cause hemolytic reactions after transfusion depending on the extent of expression of H antigen when I antigen is also present. Unlike earlier case reports, we detected and characterized anti-IH during grouping itself, hence averting a hemolytic transfusion reaction by transfusing A₁B PRBCs.^[2-6] Depending on electronic cross-match rather than conventional cross-match could place the patient at risk of being transfused

Table 1: Blood grouping at room temperature (tube method)

Anti-A	Anti-B	Anti-AB	Anti-D	A cell	B cell	O cell
4+	4+	4+	4+	w+	2+	3+

Table 2a: Blood grouping at 4°C (tube method)

Anti-A	Anti-B	Anti-AB	Anti-D	A cell	B cell	O cell
4+	4+	4+	4+	w+	2+	4+

Table 2b: Blood grouping at 37°C (tube method)

Anti-A	Anti-B	Anti-AB	Anti-D	A cell	B cell	O cell
4+	4+	4+	4+	0	0	2+

Table 3: Serologic findings in a patient with a high-thermal-amplitude, anti-IH autoantibody: Indirect Coomb's test different phases

	Immediate spin	37°C	AHG
Cell panel 1	3+	w+	w+
Cell panel 2	3+	w+	w+
Cell panel 3	3+	w+	w+

AHG: AntiHuman Globulin

Table 4a: Reaction of our patients serum to different red blood cell phenotypes

RBC phenotype	Oi _{adult}	Oh I _{adult}	Oi _{cord}	A ₁ I _{adult}	A ₂ I _{adult}
Reaction	3+	0	0	w+	3+

RBC: Red blood cell

Table 4b: Current literature on reactivity of cold agglutinins at 4°C with ABO compatible red blood cells

RBC phenotype	Anti-I	Anti-H	Anti-IH
Group OI _{adult}	4+	4+	4+
Bombay Oh I _{adult}	4+	0	0-2+
Group Oi _{cord}	0-1+	4+	0-1+
Group A1 I _{adult}	4+	0-1+	0-1+
Group A2 I _{adult}	4+	2+	2+

RBC: Red blood cell

with other subgroups (e.g. A₂ for A₁) unless the antibody picked up during grouping and antibody screening is strictly evaluated.

Conclusion

This case report illustrates the presence of an antibody (anti-IH), a cold agglutinin with broad thermal amplitude, thereby making it clinically significant. We intent to demonstrate the importance of reverse grouping for detecting this antibody and also throw light onto a scenario where O blood group becomes incompatible for A₁B individuals. This case also illustrates that clinically significant anti-IH agglutinins may occur in the apparent absence of any underlying primary hematologic disease. Uniqueness of this case report was that incompatibility with O group was detected earlier, and hence, a catastrophic transfusion reaction was subverted.

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Conflicts of interest

There are no conflicts of interest.

References

1. Harmening DM. Autoimmune hemolytic anemia. Modern Blood Banking and Transfusion Practices. 6th ed. NewDelhi: Jaypee Publication; 2013. p. 446-7.
2. Arndt P, Garratty C, Haverty D, McGrath C, Tobais P, Larison J, *et al.* Clinically significant anti-HI in two patients with greatly increased i antigen on their red cells. Blood 1997;90:2097.
3. Campbell SA, Shirey RS, King KE, Ness PM. An acute hemolytic transfusion reaction due to anti-IH in a patient with sickle cell disease. Transfusion 2000;40:828-31.
4. Darabi K, Makar RS. Acute hemolysis of transfused A2 red cells by an auto-HI antibody. Transfusion 2008;48:964-8.
5. Irani MS, Richards C. Hemolytic transfusion reaction due to anti-IH. Transfusion 2011;51:2676-8.
6. Read SM, Whiteoak EJ, Benjamin RJ. Usual IH-like antibody implicated in delayed hemolytic transfusion reaction (abstract). Transfusion 2003;43:101a.
7. Klein HG, Anstee DJ. Mollison's Blood Transfusion in Clinical Medicine. 11th ed. Malden (MA): Blackwell Publishing; 2005.
8. Petz LD, Garratty G. Immune Hemolytic Anemias. 2nd ed. Philadelphia: Churchill Livingstone; 2004. p. 182-8.
9. Klein HG, Anstee DJ. Mollison's Blood Transfusion in Clinical Medicine. 11th ed. Malden (MA): Blackwell Publishing; 2005. p. 253-60.
10. Beck ML. The I blood group collection. In: Moulds JM, Woods LI, editors. Blood Groups: P, I, Sda and Pr. Arlington: American Association of Blood Banks; 1991. p. 23-47.
11. Daniels G. Human Blood Groups. Cambridge: Blackwell; 1995. p. 74.
12. Reid ME, Lomas-Francis C. The Blood Group Antigen Facts Book. 2nd ed. London: Academic Press; 2004. p. 35-7.
13. Judd WJ. Controversies in transfusion medicine. Prewarmed tests: Con. Transfusion 1995;35:271-5.
14. Mallory D. Controversies in transfusion medicine. Prewarmed tests: Pro-why, when, and how-not if. Transfusion 1995;35:268-70.